AMENDMENT TO DRAWING FIGURES

Please replace original Sheet 1/4 submitted with the instant application with the attached Replacement Sheet 1/4. A marked-up copy of Figure 2 that is being amended with this submission is also attached and labeled as "Annotated Marked-Up Drawings".

REMARKS

Status of the Claims

Claims 1, 26-29, 48-60 and 63-82 are pending in the application.

Summary

Claims 1, 26-29, 48-60 and 63-82 are pending in the application and were examined in the Office Action dated 20 June 2005. All claims stand rejected, specifically, the Office has raised the following objections/claim rejections: **(a)** the drawings have been objected to under 37 C.F.R. §1.83(a) as failing to show every feature of the invention specified in the claims; **(b)** claim 60 stands rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement; **(c)** claims 1, 26-29, 48-49, 53, 63-71 and 75-82 have been rejected under 35 U.S.C. §103(a) as unpatentable over International Publication WO 97/38698 to Manning et al. ("Manning"); **(d)** claims 50-52 and 72-74 have been rejected under 35 U.S.C. §103(a) as unpatentable over Manning in view of U.S. Patent No. 4,472,394 to Peterson ("Peterson"); and **(d)** claims 54-59 stand rejected under 35 U.S.C. §103(a) as unpatentable over Manning. Applicants respectfully traverse all pending objections and claim rejections for the following reasons.

Overview of the Amendment

Applicants, by way of this amendment, have entered a single amendment to Figure 2. More particularly, applicants have added a second reference number 14 (as best seen in the marked-up version of the amended drawing sheet attached to this Response) to illustrate the drug delivery unit (10) having multiple carrier materials (14) depicted by the broken diagonal lines and the unmarked field in the background. Support for this amendment can be found in Figures 1 and 2 as originally filed, and in the specification at page 40, lines 2-19. Accordingly no new matter has been added by way of the amendment to Figure 2, and the entry thereof is respectfully requested.

The Objection under 37 C.F.R. §1.83(a)

The drawings have been objected to under 37 C.F.R. §1.83(a) as failing to show every feature of the invention specified in the claims. More particularly, the Office objects that the multi-phased composite drug delivery unit of claim 60 must be shown in the figures, or the feature cancelled from the claim. In response, applicants draw the Office's attention to the amendment to Figure 2 provided herewith. As can be seen, the multi-phase carrier material (14) is shown in Figure 2 as including two different materials, one depicted by the broken diagonal lines, and the other by the unmarked background of the drug delivery unit (10). As described in detail in the specification at page 40, lines 2-19, the carrier material can be a single material (e.g., see Figure 1, and see also Figure 2 where both the broken lines and the unmarked background are the same material), or alternatively there can be multiple (e.g., two) carrier materials (e.g., see Figure 2, where the broken lines and the unmarked background comprise different carrier materials). The term "multi-phase" is used by those skilled in the pharmaceutical arts to refer to a system where two different carrier materials are used in a single controlled release dosage form. Such systems can be formed using a single type of polymer (e.g., a biodegradable polyester) where two different molecular weight species of the polymer are employed, or where two different polymers are used (e.g., two different biodegradable polymers having differing dissolution characteristics to provide one or more zones that will dissolve faster than other zones. See applicants' specification at page 30, lines 28-33. Reconsideration and withdrawal of the objection to the drawings under 37 C.F.R. §1.83(a) is thus respectfully requested.

The Rejection under 35 U.S.C. §112, First Paragraph

Claim 60 stands rejected under 35 U.S.C. §112, first paragraph, on the basis of written description. No specific basis for the rejections has been provided. Applicants thus assume that the present claim rejection is grounded on the same basis as the earlier objection to the drawings. Accordingly, with regard to claim 60, applicants respectfully traverse the rejection. Accordingly, applicants draw the Office's attention to amended

Figure 2, and the accompanying disclosure from the specification at page 30, lines 28-33; and page 40, lines 6-30. Applicants further draw the Office's attention to the traversal provided herein above in response to the objection to Figure 2. As can be seen, the multi-phase carrier material (14) is shown in Figure 2 and described in sufficient detail in the specification to convey to the skilled person that applicants' had full possession of the invention as claimed at the time the application was filed. Reconsideration and withdrawal of the rejection of claim 60 under 35 U.S.C. §112, first paragraph, is thus respectfully requested.

The Rejections under 35 U.S.C. §103

Claims 1, 26-29, 48-49, 53, 63-71 and 75-82 have been rejected under 35 U.S.C. §103(a) as unpatentable over Manning. The grounds for the rejection are provided at page 3 through to the middle of page 5 of the instant Office Action. Applicants note that the instant grounds of rejection are identical to the grounds asserted in the previous Office Actions (see page 3 through to the middle of page 5 of the Action dated 27 September 2004 and page 3 through to the middle of page 5 of the Action dated 23 February 2004). However, applicants submitted amended claims in their RCE Submission of 23 July 2004, whereby the subject matter of claims 1, 26-29, 48-49, 53 and 63-70 was changed, and the specific grounds of rejection repeated in this newest Office Action clearly do not apply to those claims. In addition, applicants provided a complete traversal of the rejection in their 23 July 2004 RCE, whereby claims 1, 26-29, 48-49, 53, 63-71 and 75-82 were distinguished over these exact same grounds of rejection. For some reason, the Office has failed to take note of applicants' previously submitted claim amendments and traversal arguments and has likewise failed to answer the substance thereof. Accordingly, applicants again restate their traversal of the rejection as already presented in the previous two responses filed in this case, and respectfully traverse the rejection for the following additional reasons.

At page 3 of the instant Office Action, the Office asserts "Manning disclose a drug delivery unit ... that is placed such that it substantially contacts the round membrane [and] this would encompass the being in direct contact or against and 'at least partially in

said round window niche." However, applicants' claim 1 (amended with the 23 July 2004 RCE Submission) recites a method whereby a drug delivery unit is inserted directly into the round window niche and positioned completely within the round window niche. Claims 26-29, 48-49, 53 and 63-70 all depend from claim 1 and thus contain the same base limitations. A copy of the claims as currently pending has been supplied with this Response for the convenience of the Office.

As can be seen, the Office's assertion that Manning's flooding of the middle ear with a volume of liquid that fills at least one quarter of the entire middle ear "encompasses" applicants recited method is clearly wrong. Manning does not teach or disclose insertion of a drug unit directly into the subject niche, rather Manning floods the middle ear and lets some of the therapeutic eventually reach the niche. Manning likewise does not teach or disclose positioning a drug unit completely within the niche. As applicants pointed out in the traversal provided with the 23 July 2004 RCE Submission, the majority of the therapeutic administered by Manning will not be contained within the round window niche, and it therefore will not even contact the round window membrane. As further pointed out in the RCE Submission, Manning's methodology is not efficient in that majority of the therapeutic drains out of the middle ear within the first day of delivery, and Manning's methodology is not safe in that a very large amount of the therapeutic is administered to other parts of the middle ear where toxic agents can cause actual harm to the sensitive middle ear tissue. As discussed in the RCE Submission, applicants' claimed methods are a significant improvement over the art such as Manning, where a therapeutic can now be very specifically inserted directly into the target niche, avoiding potential inadvertent and harmful delivery to other tissue (important if ototoxic compositions are used), and ensuring direct delivery through the round window membrane for the duration of the controlled delivery event (hours, days, or even months). Applicants' recited methods are neither taught nor suggested in any way by the Manning reference.

Since the Office has failed to properly address applicants' amended claims, traversals and asserted advantages in two successive Office Actions on the merits, applicants submit that the Office has failed to rebut applicants' traversal. See *In re Soni*,

34 USPQ2d 1684 (Fed. Cir. 1995). Applicants thus respectfully request that the Office either immediately withdraw the improper rejection of claims 1, 26-29, 48-49, 53 and 63-70 under 35 U.S.C. §103(a), or that the Office provide yet a further new, non-final Action on the merits pursuant to 37 C.F.R. §§1.114 and 1.104. This is the second time that applicants have asked the Office to properly consider their RCE Submission.

Applicants' claim 71 (presented with the 23 July 2004 RCE Submission) recites a method whereby a drug delivery unit is inserted directly into the round window niche and positioned either partially or completely within the round window niche, wherein the unit is configured as a pellet, disk, tablet, plate, sphere, cube, cylindrical unit, strand, paste, or amorphous mass. Claims 75-82 depend from claim 71 and thus contain the same base limitations. Here again, applicants have already established that Manning does not teach or disclose insertion of a drug unit directly into the subject niche (Manning floods the middle ear and lets some of the therapeutic eventually reach the niche). Manning likewise does not teach or disclose delivery of a drug unit configured as a pellet, disk, tablet, plate, sphere, cube, cylindrical unit, strand, paste, or amorphous mass.

When considering the patentability of claims under Section 103, the claimed invention must be considered as a whole, the reference(s) must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination, the reference(s) must be viewed with the benefit of impermissible hindsight vision afforded by the claimed invention; and a reasonable expectation of success is the standard with which obviousness is determined. *Hodosh v. Block Drug Co., Inc.*, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986). Therefore, it is clear that in order to establish obviousness, the cited prior art must enable a person of ordinary skill to make and use the invention (*see: In re Kumar*, CAFC 04-1074, (decided 15 August 2005) and *Beckman Instruments, Inc. v. LKB Produkter AB*, 892 F.2d 1547 (Fed. Cir. 1989); *see also: Motorola, Inc. v. Interdigital Tech. Corp.*, 121 F.3d 1461 (Fed. Cir. 1997) and *In re Payne*, 606 F.2d 303 (CCPA 1979), and that a two-part test must be used to assess obviousness--where an appropriate teaching or suggestion must first be found in the prior art itself, and then a proper consideration must be made to assess whether or not the prior art actually enables the recited subject matter.

Manning fails both prongs of the two-part test for obviousness. Manning does not teach the placement of drug delivery unit directly into the round window niche. As established herein above and in applicants' RCE Submission, this feature provides significant efficiency and safety advantages. Even though Manning would presumably have been aware of the issues of safety (toxicity) and efficiency, Manning completely failed to teach or suggest applicants' recited methodology. This is strong and compelling evidence of non-obviousness. Since Manning failed to teach or suggest placement of drug delivery unit directly into the round window niche, and instead taught flooding of a large portion of the entire middle ear instead, it cannot possibly have enabled applicants' recited methods. An utter lack of any teaching or suggestion cannot possibly be considered enabling. In like manner, Manning failed to teach or suggest configuration of a drug delivery unit as a pellet, disk, tablet, plate, sphere, cube, cylindrical unit, strand, paste, or amorphous mass. Instead, Manning chose to use liquids to flood the middle ear.

For all of the foregoing reasons, then, the rejection of claims 71 and 75-82 under 35 U.S.C. §103(a) is improper. The Office has simply failed to identify any teaching or suggestion in Manning that would lead to applicants' recited methodology. There is nothing in the grounds of rejection recited at page 3 through the middle of page 5 of the instant Office Action that even addresses the difference between Manning and applicants' claims. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

Claims 50-52 and 72-74 stand rejected under 35 U.S.C. §103(a) as unpatentable over Manning in view of Peterson. The specific grounds for the rejection are provided at page 5 of the instant Office Action. Here again, applicants note that the instant grounds of rejection are identical to the grounds asserted in the previous Office Actions (see page 5 of the Action dated 27 September 2004 and page 5 of the Action dated 23 February 2004); and therefore applicants' traversal provided with the RCE Submission has simply not been considered or answered. Accordingly, applicants again restate their traversal of the rejection as already presented in the previous two responses filed in this case, and respectfully traverse the rejection for the following additional reasons.

The Office has looked to the primary reference (Manning) as discussed above, and then seeks to supplement this with the addition of the secondary reference (Peterson)

to teach implantation of a controlled release composition beneath the ear of a domestic farm animal. As applicants pointed out in the July 2004 RCE Submission, Peterson teaches implantation of a systemic weight gain substance into a farm animal (cows, pigs and lambs). For farm animals that are raised for human consumption, the ear provides a convenient location for implantation of medicines. Initially, the ear is not generally consumed, so drugs will not enter into human consumption. In addition, the ear provides a convenient target since it is a rather large tissue, it is readily accessible, and has very little to no nerve endings. Manning relates to treatment of human ear disorders by use of locally active drugs. The skilled ear treatment professional, considering how to modify Manning would never consider the Peterson reference. It relates to an entirely different problem (how to administer systemic medications to farm animals by implanting a drug in the pendulant ear tissue flap of a farm animal). Adding Peterson to Manning still fails to teach or suggest direct administration of a drug unit into the round window niche where the unit is positioned completely within the round window niche (claims 5-52); nor does it teach or suggest direct administration of a drug unit into the round window niche where the unit is configured as a pellet, disk, tablet, plate, sphere, cube, cylindrical unit, strand, paste, or amorphous mass (claims 72-74). The advantages (safety and efficiency) were clearly set out in applicants' RCE submission. Since the Office has failed to properly address applicants' amended claims, traversals and asserted advantages in two successive Office Actions on the merits, applicants submit that the Office has failed to rebut applicants' traversal. See *In re Soni*, 34 USPQ2d 1684 (Fed. Cir. 1995). Applicants thus respectfully request that the Office either immediately withdraw the improper rejection of claims 50-52 and 72-74 under 35 U.S.C. §103(a), or that the Office provide yet a further new, non-final Action on the merits pursuant to 37 C.F.R. §§1.114 and 1.104. Here again, this is the second time that applicants have asked the Office to properly consider their RCE Submission.

In addition to the traversal previously submitted in this case, applicants submit that the combination of Manning and Peterson fails the two-part test for obviousness. Neither Manning nor Peterson teach the placement of drug delivery unit directly into the round window niche. As established herein above and in applicants' RCE Submission,

this feature provides significant efficiency and safety advantages. Since both Manning and Peterson fail to teach or suggest placement of drug delivery unit directly into the round window niche, this improper combination cannot possibly have enabled applicants' recited methods.

For all of the foregoing reasons, then, the rejection of claims 50-52 and 72-74 under 35 U.S.C. §103(a) is improper. The Office has simply failed to identify any teaching or suggestion in its recited combination that would lead to applicants' recited methodology. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

Finally, claims 54-59 stand rejected under 35 U.S.C. §103(a) as unpatentable over Manning. The specific grounds for the rejection are provided at page 6 of the instant Office Action. Here again, applicants note that the instant grounds of rejection are identical to the grounds asserted in the previous Office Actions (see page 6 of the Action dated 27 September 2004 and page 6 of the Action dated 23 February 2004); and therefore applicants' traversal provided with the RCE Submission has simply not been considered or answered. Accordingly, applicants again restate their traversal of the rejection as already presented in the previous two responses filed in this case, and for the following additional reasons.

As applicants pointed out in the July 2004 RCE Submission, Manning does not teach or disclose insertion of a drug unit directly into the subject niche, rather Manning floods the middle ear and lets some of the therapeutic eventually reach the niche. Manning likewise does not teach or disclose positioning a drug unit completely within the niche. The advantages (safety and efficiency) were clearly set out in applicants' RCE submission. Since the Office has failed to properly address applicants' amended claims, traversals and asserted advantages in two successive Office Actions on the merits, applicants submit that the Office has failed to rebut applicants' traversal. See *In re Soni*, 34 USPQ2d 1684 (Fed. Cir. 1995). Applicants thus respectfully request that the Office either immediately withdraw the improper rejection of claims 54-59 under 35 U.S.C. §103(a), or that the Office provide yet a further new, non-final Action on the merits pursuant to 37 C.F.R. §§1.114 and 1.104. Here again, this is the second time that applicants have asked the Office to properly consider their RCE Submission.

In addition to the traversal previously submitted in this case, applicants submit that Manning fails the two-part test for obviousness (in order to establish obviousness, the cited prior art must enable a person of ordinary skill to make and use the invention (*see: In re Kumar*, CAFC 04-1074, (decided 15 August 2005) and *Beckman Instruments, Inc. v. LKB Produkter AB*, 892 F.2d 1547 (Fed. Cir. 1989); *see also: Motorola, Inc. v. Interdigital Tech. Corp.*, 121 F.3d 1461 (Fed. Cir. 1997) and *In re Payne*, 606 F.2d 303 (CCPA 1979)). Manning quite simply fails to teach or suggest the placement of drug delivery unit directly into the round window niche. This feature of applicants' recited methods provides significant efficiency and safety advantages. Even though Manning would presumably have been aware of the issues of safety (toxicity) and efficiency, Manning completely failed to teach or suggest applicants' claimed methods. This is strong and compelling evidence of non-obviousness. Since Manning failed to teach or suggest placement of drug delivery unit directly into the round window niche, and instead taught flooding of a large portion of the entire middle ear instead, it cannot possibly have enabled applicants' recited methods. An utter lack of any teaching or suggestion cannot possibly be considered to be an enabling disclosure.

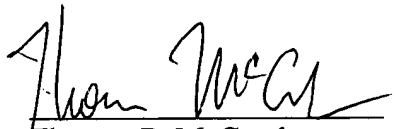
For all of the foregoing reasons, then, the rejection of claims 54-59 under 35 U.S.C. §103(a) is improper. The Office has simply failed to identify any teaching or suggestion in Manning that would lead to applicants' recited methodology. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

CONCLUSION

Applicants submit that the pending claims define an invention that is both novel and nonobvious over the cited art, and thus all claims are in condition for allowance. Acknowledgement of this by the Office in the form of an early allowance is thus respectfully requested. In addition, if the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, applicants invite the Examiner to contact the undersigned at (408) 777-4915.

The appropriate fee is attached or authorized. If the Commissioner determines that an additional fee is necessary, the Commissioner is hereby authorized to charge any additional fees associated with this communication or credit any overpayment to Deposit Account No. **50-1953.**

Respectfully submitted,



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